

*sub E*  
108. The method of claim 104 wherein the gene is selected from the group consisting of: ganB, gpa3, creA, Lys14, and Pc23.

109. The method of claim 104 wherein the modulation is overexpression of the gene.

110. The method of claim 104 wherein the modulation is conditional expression of the gene.

*D* 111. The method of claim 104 wherein the modulation comprises a dominant negative mutation in the gene. *E*

112. The method of claim 104 wherein the modulation comprises a dominant positive mutation in the gene.

113. The method of claim 107 wherein the fungus is *A. terreus*.

114. The method of claim 104 wherein the gene is selected from the group consisting of ganB and fungal homologs thereof.

115. The method of claim 104 wherein the gene is selected from the group consisting of gpa3 and fungal homologs thereof.

*E* 116. The method of claim 104 wherein the gene is selected from the group consisting of creA and fungal homologs thereof.

117. The method of claim 104 wherein the gene is selected from the group consisting of Lys14 and fungal homologs thereof.

118. The method of claim 104 wherein the gene is selected from the group consisting of Pc23 and fungal homologs thereof.

119. The method of claim 104 wherein the yield of polyketide by the fungus is increased.

*Sub E1*  
120. A method for providing a fungal cell with improved polyketide production, the method comprising transforming a fungal cell with a nucleic acid molecule comprising a nucleotide sequence encoding a protein selected from the group consisting of: ganB, gpa3, creA, Lys14 and Pc23 and fungal homologs thereof.

*D*  
121. The method of claim 120 wherein the polyketide is a statin.

122. The method of claim 121 wherein the statin is lovastatin.

123. The method of claim 120 wherein the fungus is an Ascomycetes.

*Sub E1*  
124. The method of claim 120 wherein the protein is selected from the group consisting of: ganB, gpa3, creA, Lys14 and Pc23.

125. The method of claim 123 wherein the fungus is *A. terreus*.

126. The method of claim 120 wherein the gene is selected from the group consisting of ganB and fungal homologs thereof.

127. The method of claim 120 wherein the gene is selected from the group consisting of gpa3 and fungal homologs thereof. *E*

128. The method of claim 120 wherein the gene is selected from the group consisting of creA and fungal homologs thereof.

129. The method of claim 120 wherein the gene is selected from the group consisting of Lys14 and fungal homologs thereof.

130. The method of claim 120 wherein the gene is selected from the group consisting of Pc23 and fungal homologs thereof. ~~E~~

131. The method of claim 120 wherein the yield of polyketide by the transformed fungus is greater than the yield of polyketide by the non-transformed fungus.

~~132. A genetically modified fungus having the ability to produce a polyketide wherein the production of lovastatin by the fungus has been modulated by a method comprising modulating the expression of a gene selected from the group consisting of: ganB, gpa3, creA, Lys14, Pc23 and fungal homologs thereof.~~

133. The genetically modified fungus of claim 132 wherein the polyketide is a statin.

134. The genetically modified fungus of claim 133 wherein the statin is lovastatin.

135. The genetically modified fungus of claim 132 wherein the fungus is an Ascomycetes.

~~136. The genetically modified fungus of claim 132 wherein the gene is selected from the group consisting of: ganB, gpa3, creA, Lys14, and Pc23.~~

137. The genetically modified fungus of claim 135 wherein the fungus is *A. terreus*.

138. The genetically modified fungus of claim 132 wherein the gene is selected from the group consisting of ganB and fungal homologs thereof. ~~E~~

139. The genetically modified fungus of claim 132 wherein the gene is selected from the group consisting of gpa3 and fungal homologs thereof.

140. The genetically modified fungus of claim 132 wherein the gene is selected from the group consisting of creA and fungal homologs thereof.

141. The genetically modified fungus of claim 132 wherein the gene is selected from the group consisting of Lys14 and fungal homologs thereof.

142. The genetically modified fungus of claim 132 wherein the gene is selected from the group consisting of Pc23 and fungal homologs thereof.

143. The genetically modified fungus of claim 132 wherein the yield of a polyketide by the transformed fungus is greater than the yield of a polyketide by the non-transformed fungus.

144. A method for producing a polyketide, the method comprising culturing a genetically modified fungus according to claim 132 in culture medium under conditions suitable for the production of the polyketide.

145. The method of claim 144 wherein the polyketide is a statin.

146. The method of claim 145 wherein the statin is lovastatin.

147. The method of claim 144 wherein the fungus is an Ascomycetes.

148. The method of claim 144 further comprising isolating a fraction of culture medium containing a polyketide.

149. A polyketide produced by the method of claim 148.

150. A method for modulating the production of a secondary metabolite by a fungus, the method comprising modulating the expression of a gene selected from the group consisting

of: creA, lovE, pacC and fungal homologs thereof, provided however, that when the secondary metabolite is lovastatin, the gene is not lovE and that when the secondary metabolite is penicillin, the gene is not pacC.

151. The method of claim 150 wherein the secondary metabolite is a polyketide.

152. The method of claim 151 wherein the polyketide is a statin.

153. The method of claim 152 wherein the statin is lovastatin.

154. The method of claim 151 wherein the secondary metabolite is a  $\beta$ -lactam.

155. The method of claim 154 wherein the  $\beta$ -lactam is penicillin.

156. The method of claim 152 wherein the fungus is an Ascomycetes.

157. The method of claim 156 wherein the fungus is *A. terreus*.

158. The method of claim 156 wherein the fungus is *P. chrysogenum*.

159. The method of claim 150 wherein the gene selected from the group consisting of: creA, lovE, pacC, provided however, that when the secondary metabolite is lovastatin, the gene is not lovE and that when the secondary metabolite is penicillin, the gene is not pacC.

160. The method of claim 150 wherein the modulation is overexpression of the gene.

161. The method of claim 150 wherein the modulation is conditional expression of the gene.

162. The method of claim 150 wherein the modulation comprises a dominant negative mutation in the gene.

163. The method of claim 150 wherein the modulation comprises a dominant positive mutation in the gene.

164. The method of claim 150 wherein the modulation comprises a dominant neomorphic mutation in the gene.

165. The method of claim 150 wherein the gene is selected from the group consisting of creA and fungal homologs thereof.

166. The method of claim 150 wherein the gene is selected from the group consisting of lovE and fungal homologs thereof.

167. The method of claim 150 wherein the gene is selected from the group consisting of pacC and fungal homologs thereof.

168. A method for providing a fungal cell with improved secondary metabolite production, the method comprising transforming a fungal cell with a nucleic acid molecule comprising a nucleotide sequence encoding a protein selected from the group consisting of creA, lovE, pacC and fungal homologs thereof, provided however, that when the secondary metabolite is lovastatin, the protein is not lovE and that when the secondary metabolite is penicillin, the protein is not pacC.

169. The method of claim 168 wherein the secondary metabolite is a polyketide.

170. The method of claim 169 wherein the polyketide is a statin.

171. The method of claim 170 wherein the statin is lovastatin.

172. The method of claim 168 wherein the secondary metabolite is a  $\beta$ -lactam.
173. The method of claim 172 wherein the  $\beta$ -lactam is penicillin.
174. The method of claim 168 wherein the fungus is an Ascomycetes.
175. The method of claim 174 wherein the fungus is *A. terreus*.
176. The method of claim 174 wherein the fungus is *P. chrysogenum*.
177. The method of claim 168 wherein the protein is selected from the group consisting of: creA, lovE, and pacC, provided however, that when the secondary metabolite is lovastatin, the protein is not lovE and that when the secondary metabolite is penicillin, the protein is not pacC.
178. The method of claim 168 wherein the gene is selected from the group consisting of creA and fungal homologs thereof. *E*
179. The method of claim 168 wherein the gene is selected from the group consisting of lovE and fungal homologs thereof.
180. The method of claim 168 wherein the gene is selected from the group consisting of pacC and fungal homologs thereof.
181. A method for modulating the production of a  $\beta$ -lactam by a fungus, the method comprising modulating the expression of a gene selected from the group consisting of: creA, lovE, AAD34561 and fungal homologs thereof.
182. The method of claim 181 wherein the fungus is an Ascomycetes.

183. The method of claim 182 wherein the fungus is *A. terreus*.

184. The method of claim 181 wherein the modulation comprises a dominant negative mutation in the gene.

185. The method of claim 181 wherein the modulation comprises a dominant positive mutation in the gene.

186. The method of claim 181 wherein the modulation comprises a dominant neomorphic mutation in the gene.

187. The method of claim 181 wherein the gene is selected from the group consisting of: creA, love and AAD34561,

188. The method of claim 181 wherein the modulation is overexpression of the gene.

189. The method of claim 181 wherein the modulation is conditional expression of the gene.

190. The method of claim 182 wherein the fungus is *P. chrysogenum*.

191. The method of claim 181 wherein the gene is selected from the group consisting of creA and fungal homologs thereof.

192. The method of claim 181 wherein the gene is selected from the group consisting of lovE and fungal homologs thereof.

193. The method of claim 181 wherein the gene is selected from the group consisting of AAD34561 and fungal homologs thereof.



194. The method of claim 181 wherein the yield of a  $\beta$ -lactam by the fungus is increased.

195. The method of claim 181 wherein the  $\beta$ -lactam is penicillin.

196. A method for providing a fungal cell with improved  $\beta$ -lactam production, the method comprising transforming a fungal cell with a nucleic acid molecule comprising a nucleotide sequence encoding a protein selected from the group consisting of creA, lovE, AAD34561 and fungal homologs thereof.

197. The method of claim 196 wherein the protein is selected from the group consisting of creA, lovE, and AAD34561

198. The method of claim 196 wherein the gene is selected from the group consisting of creA and fungal homologs thereof.

199. The method of claim 196 wherein the gene is selected from the group consisting of lovE and fungal homologs thereof.

200. The method of claim 196 wherein the gene is selected from the group consisting of AAD34561 and fungal homologs thereof.

201. The method of claim 196 wherein the yield of a  $\beta$ -lactam by the fungus is increased.

202. The method of claim 196 wherein the  $\beta$ -lactam is penicillin.

203. The method of claim 196 wherein the fungus is an Ascomycetes.

204. The method of claim 203 wherein the fungus is *A. terreus*.

205. The method of claim 203 wherein the fungus is *P. chrysogenum*.

206. A genetically modified fungus having the ability to produce a  $\beta$ -lactam wherein the production of a  $\beta$ -lactam by the fungus has been modulated by a method comprising modulating the expression of a gene selected from the group consisting of: creA, lovE, AAD34561 and fungal homologs thereof.

207. The genetically modified fungus of claim 206 wherein the gene is selected from the group consisting of: creA, lovE, and AAD34561.

208. The genetically modified fungus of claim 206 wherein the modulation comprises a dominant negative mutation in the gene.

209. The genetically modified fungus of claim 206 wherein the modulation comprises a dominant positive mutation in the gene.

210. The method of claim 206 wherein the modulation comprises a dominant neomorphic mutation in the gene.

211. The genetically modified fungus of claim 206 wherein the modulation is overexpression of the gene.

212. The genetically modified fungus of claim 206 wherein the modulation is conditional expression of the gene.

213. The genetically modified fungus of claim 206 wherein the gene is selected from the group consisting of creA and fungal homologs thereof.

214. The genetically modified fungus of claim 206 wherein the gene is selected from the group consisting of lovE and fungal homologs thereof.

215. The genetically modified fungus of claim 206 wherein the gene is selected from the group consisting of AAD34561 and fungal homologs thereof.

216. The genetically modified fungus of claim 206 wherein the yield of a  $\beta$ -lactam by the fungus is increased.

217. The genetically modified fungus of claim 206 wherein the  $\beta$ -lactam is penicillin.

218. The genetically modified fungus of claim 206 wherein the fungus is an Ascomycetes.

219. The genetically modified fungus of claim 218 wherein the fungus is *A. terreus*.

220. The genetically modified fungus of claim 218 wherein the fungus is *P. chrysogenum*.

221. The genetically modified fungus of claim 206 wherein the yield of a  $\beta$ -lactam by the transformed fungus is greater than the yield of a  $\beta$ -lactam by the non-transformed fungus.

222. A method for producing a  $\beta$ -lactam, the method comprising culturing a genetically modified fungus according to any of claims 206 in culture medium under conditions suitable for the production of a  $\beta$ -lactam.

223. The method of claim 222 further comprising isolating a fraction of culture medium containing a  $\beta$ -lactam.

224. A  $\beta$ -lactam produced by the method of claim 223.--